Evaluation of bowel distension and mural visualisation using neutral oral contrast agents for multidetector-row computed tomography

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INTRODUCTION We compared the effectiveness of different types of non-commercial neutral oral contrast agents for bowel distension and mural visualisation in computed tomographic (CT) enterography.

METHODS 90 consecutive patients from a group of 108 were randomly assigned to receive water (n = 30), 3.8% milk (n = 30) or 0.1% gastrografin (n = 30) as oral contrast agent. The results were independently reviewed by two radiologists who were blinded to the contrast agents used. The degree of bowel distension was qualitatively scored on a four-point scale. The discrimination of bowel loops, mural visualisation and visualisation of mucosal folds were evaluated on a 'yes' or 'no' basis. Side effects of the various agents were also recorded.

RESULTS 3.8% milk was significantly superior to water for bowel distension (jejunum, ileum and terminal ileum), discrimination of bowel loops (jejunum and ileum), mural visualisation and visualisation of mucosal folds (ileum and terminal ileum). It was also significantly superior to 0.1% gastrografin for bowel distension, discrimination of bowel loops, mural visualisation and visualisation of mucosal folds (jejunum, ileum and terminal ileum). However, 10% of patients who received 3.8% milk reported immediate post-test diarrhoea. No side effects were documented for patients who received water and 0.1% gastrografin.

CONCLUSION 3.8% milk is an effective and superior neutral oral contrast agent for the assessment of the jejunum, ileum and terminal ileum in CT enterography. However, further studies are needed to explore other suitable oral contrast agents for CT enterography in lactose- or cow's milk-intolerant patients.

Keywords: bowel distension, CT enterography, imaging, mural visualisation, neutral oral contrast
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INTRODUCTION

Positive or high-attenuation oral contrast agents have traditionally been used in abdominal computed tomography (CT) imaging. However, for small bowel imaging, positive contrast agents are generally not preferred because they mask the enhancement of the mucosa and lesions such as neuroendocrine tumours. In the mid-1980s, neutral oral contrast agents began to be explored for use in cross-sectional small bowel imaging.[1] Recent advances in CT technology have introduced a new the cross-sectional imaging technique that is specific for the small bowel, known as CT enterography. It combines neutral or low-attenuation oral contrast agents with intravenous contrast to optimally assess diseases of the small bowel. With this technique, inflammatory bowel diseases, small bowel vascular malformations, ischaemia, sprue and tumours have been detected.[2]

Our goal was to determine a universal oral contrast agent that could provide optimal small bowel luminal distension and mural visualisation for the assessment and detection of signs of inflammatory bowel disease. The purpose of this study was to evaluate the utility of milk and diluted gastrografin as low-attenuation oral contrast agents for bowel imaging in multidetector-row CT (MDCT), by comparing the results of 3.8% milk and 0.1% gastrografin to that of water.

METHODS

This study was approved by the medical ethics committee at University of Malaya Medical Centre, Kuala Lumpur, Malaysia. In this blinded prospective study, consecutive patients who underwent contrast-enhanced CT of the abdomen and pelvis from November 2008 to October 2009 were recruited. The study population comprised 108 patients who were referred for and underwent contrast-enhanced CT abdomen and pelvis for indications other than bowel-related disease, and who had no previous history of bowel surgery. The inclusion criteria were patients aged ≥ 15 years who were referred for MDCT of the abdomen and pelvis. Patients with a history of bowel-related disease or bowel surgery and those with CT findings of bowel-related disease were excluded from the study. This was to ensure that the reproducible concentration and amount of oral contrast was steadily achievable on 'normal' subjects prior to extending it to other patients, such as those with Crohn's disease. Also excluded from the study were patients who had CT findings of an intra-abdominal mass that may cause mass effect to the portion of the examined bowel, images that were degraded by breathing or motion artefact, delay in CT examination time (of more than one hour following the intake of the first dose of oral contrast agent), a history of lactose or cow's milk intolerance,

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contraindication to iodinated contrast media, and those who were pregnant.

All the patients fasted for at least six hours prior to the CT examination. Contraindications to the contrast injection were ruled out, and written informed consent was obtained for the administration of intravenous and oral contrast materials. A 20G cannula was placed in each patient's antecubital vein. A volume of 600 mL of oral contrast agent was ingested 40–60 minutes before imaging, and an additional 400 mL was ingested 20 minutes before imaging by all patients. The patients were divided into three groups. Patients from group 1 were given water, group 2 received 3.8% milk (milk with 3.8% fat) and group 3 were given 0.1% gastrografin. For the 3.8% milk, fresh milk in a sealed Tetra Pak (1 L) was used. All milk was kept in a refrigerator and one pack (1 L) was used for each patient. There was no leftover milk.

Imaging of all the patients were performed using a Siemens Somatom Sensation 16-slice MDCT scanner (Medical Solutions, Forchheim, Germany), with the following scan parameters: 300–350 mA, 120 kVp and beam collimation of 12 mm (0.75 × 16 mm^2). 100 mL of iopromide 300 mg/mL (Ultravist, Schering AG, Germany), was administered intravenously using a power injector at the rate of 2 mL/sec for all the patients. The patients were instructed to hold their breath at full inspiration during scanning. CT images in the portovenous phase (60-second delay after contrast injection) were obtained. During post-processing, images were reconstructed into coronal 1.5-mm sections. No intravenous glucagon or metoclopramide hydrochloride was administered, as we had found from a pilot study consisting of five patients that these agents were not useful, as they showed poor bowel distension. Side effects of the different types of oral contrast agent (water, 3.8% milk, 0.1% gastrografin) were recorded via direct questioning of the patients within ten minutes of termination of the CT examination. Patients were also told to report any side effects, including abdominal discomfort, abdominal cramping, nausea, vomiting, flatulence and diarrhoea, occurring at home on the day of the examination.

Images in the coronal 1.5-mm sections were reviewed independently by two attending radiologists in a soft tissue window via a picture archiving and communication system workstation. Coronal images were used to simulate the effect of viewing the subject during the process of enteroclysis. Another reason for this approach was that it is easier to pinpoint the anatomical location on coronal imaging than on axial imaging, especially beyond the D-J flexure. Both radiologists were blinded to the type of oral contrast agents used. Images from each examination were evaluated for selected parts of the gastrointestinal tract, which included the duodenum, jejunum and ileum. The different parts of the duodenum (second, third and fourth parts) were assessed separately. As the jejunum and ileum comprise long segments of bowel, assessments of three parts (proximal, middle and distal segments) were done, and the mean from these three selected assessments were taken as a single score. As the terminal ileum is the commonest site for Crohn's disease, accuracy in the assessment of this segment of the bowel is crucial as the mean score from the rest of the ileum may not be representative of this segment. Therefore, the terminal ileum was assessed separately from the rest of the ileum.

A four-point scale was used for scoring bowel distension, and the luminal diameter (in cm) of the bowel assessed was noted (4 = excellent distension [> 2 cm]; 3 = good partial distension [1–2 cm]; 2 = minimal distension [1 cm]; 1 = complete bowel collapse).[3] In the case of the jejunum and ileum, the mean scores of the proximal, middle and distal segments were given as a round figure. The discrimination of bowel loops, visualisation of bowel wall and visualisation of mucosal folds were evaluated on a 'yes' or 'no' basis. Discrimination of bowel loops was defined according to the reviewer's ability to identify each bowel loop and separately from the adjacent intra-abdominal organs. Visualisation of bowel wall and mucosal folds was defined as the reviewer's ability to delineate the bowel wall and mucosal folds from the bowel lumen, and to measure their thickness. In the case of the jejunum and ileum, where three selected segments (proximal, middle and distal) were evaluated, a single score of 'yes' or 'no' was determined from similar scores given to two or more segments. The grades received from each reviewer were averaged for each patient, and the mean of the grades from the two reviewers was used as a single score.

The Mann-Whitney U test was used to evaluate for any statistically significant difference between the three oral contrast agents (milk vs. gastrografin, milk vs. water, water vs. gastrografin) for bowel distension. The chi-square test was used for discriminating between bowel loops, mural visualisation and visualisation of mucosal folds. The Bonferroni correction was applied. A p-value ≤ 0.017 (0.05 divided by 3) was considered to be statistically significant. For interobserver agreement, the kappa coefficient was calculated for bowel distension, discrimination of bowel loops, mural visualisation and visualisation of mucosal folds.

RESULTS

Of the 108 patients who underwent CT examination, 18 were excluded from the study. Of these, two patients had CT findings of bowel-related disease, two had previous bowel surgery and three had an intra-abdominal mass that caused mass effect to the examined bowel. Eight patients were excluded due to a delay in the CT scanning time following oral contrast administration, and three patients were excluded due to motion or breathing artefacts in the relevant images. The remaining 90 patients who underwent CT enterography fulfilled the inclusion criteria and were enrolled in the study.

Eight (27%) men and 22 (73%) women received water, seven (23%) men and 23 (77%) women received 3.8% milk, and nine (30%) men and 21 (70%) women received 0.1% gastrografin as the oral contrast agent. The mean age of the patients who received water was 55.3 ± 14.1 (range 27–81) years, that for patients who were given 3.8% milk was 50.1 ± 11.6 (range 27–71) years and

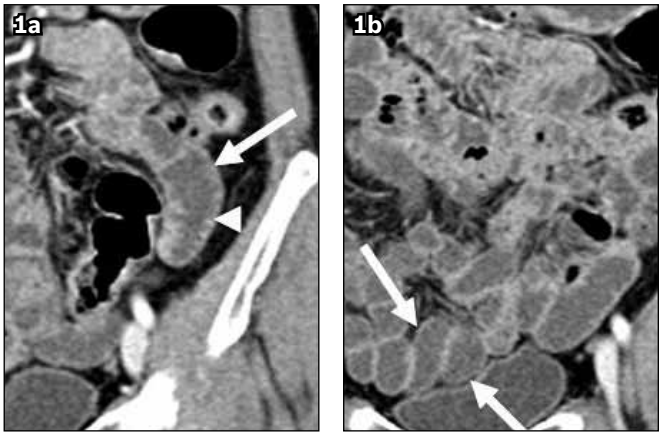

Fig. 1 Abdominal CT images of a 56-year-old woman who received 3.8% milk as an oral contrast agent. (a) Grade 3 bowel distension (white arrow), and good mural and mucosal fold visualisations (white arrowhead) are seen for the jejunum. (b) Good discrimination of the bowel loops (white arrows) is seen for the ileum.

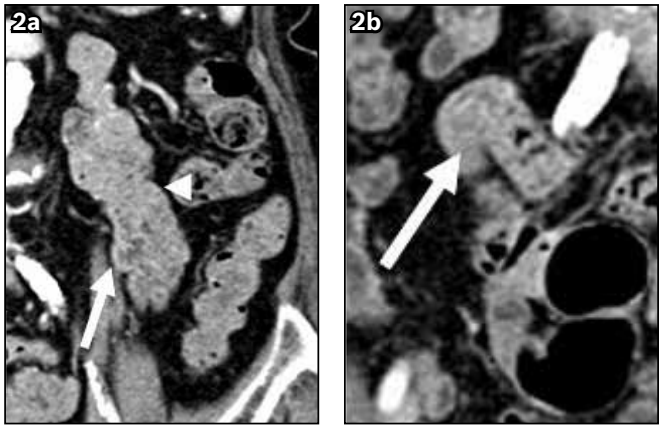

Fig. 2 Abdominal CT images of an 81-year-old woman who received water as an oral contrast agent. (a) Grade 2 bowel distension (white arrow) and poor discrimination of the bowel loops (white arrowhead) are seen for the jejunum. (b) Poor mural and mucosal fold visualisations (white arrow) are seen for the ileum.

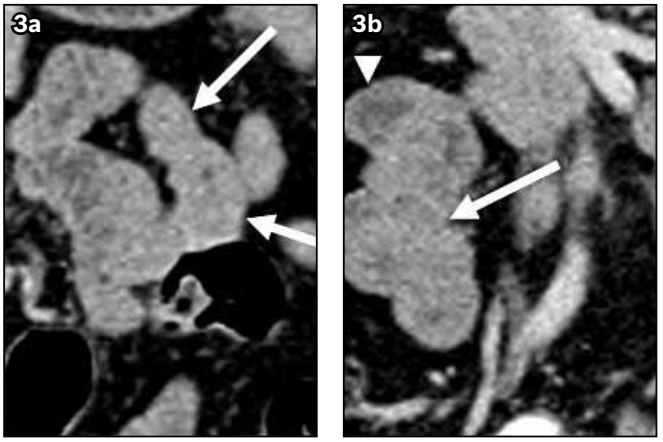

Fig. 3 Abdominal CT images of a 46-year-old woman who received 0.1% gastrografin as an oral contrast agent. (a) Poor mural and mucosal fold visualisations (white arrows) are seen for the jejunum. (b) Grade 2 bowel distension (white arrowhead) and poor discrimination of the bowel loops (white arrow) are seen for the ileum.

that for patients who received 0.1% gastrografin was 53.0 ± 13.5 (range 15–80) years.

Generally, 3.8% milk (Fig. 1) showed better bowel distension, discrimination of bowel loops, mural visualisation and visualisation of mucosal folds compared to water (Fig. 2) and 0.1% gastrografin (Fig. 3). Water was superior to 0.1% gastrografin for discrimination of the bowel loops and mural visualisation for the ileum. Aside from this, there was no significant difference, in terms of bowel distension and visualisation of mucosal folds, between water and 0.1% gastrografin as oral contrast agents.

Where bowel distension by location was concerned, 3.8% milk was significantly superior for the discrimination of the jejunum, ileum and terminal ileum compared to both water and 0.1% gastrografin. However, the grades with 3.8% milk were not significantly different from those with water and 0.1% gastrografin for the D2, D3 and D4 segments of the duodenum. There was no significant difference between the grades received with water and 0.1% gastrografin for any of the bowel segments. As an oral contrast agent, 3.8% milk was significantly superior to water for the discrimination of bowel loops in the jejunum and ileum, as well as for the jejunum, ileum and terminal ileum when compared to 0.1% gastrografin. However, there was no significant difference between 3.8% milk and water for the D2, D3 and D4 segments of the duodenum and terminal ileum, or between 3.8% milk and 0.1% gastrografin for these duodenal segments. Between water and 0.1% gastrografin, water provided significantly better discrimination of bowel loops in the ileum. Apart from the above, there was no significant difference between water and 0.1% gastrografin as oral contrast agents for the rest of the bowel.

For mural visualisation, 3.8% milk was significantly superior to water for the ileum and terminal ileum. It was also significantly superior to 0.1% gastrografin for the jejunum, ileum and terminal ileum. There was no significant difference between 3.8% milk and water for the D2, D3 and D4 segments of the duodenum and jejunum or between 3.8% milk and 0.1% gastrografin for the same duodenal segments. With the exception of the ileum, where water showed significantly better mural visualisation than 0.1% gastrografin, there was no significant difference between the two oral contrast agents for the rest of the bowel. 3.8% milk showed significantly better visualisation of the mucosal folds in the ileum and terminal ileum compared to water. It was also significantly superior to 0.1% gastrografin for the jejunum, ileum and terminal ileum. However, there was no significant difference between 3.8% milk and water for the D2, D3 and D4 segments of the duodenum and jejunum, or between 3.8% milk and 0.1% gastrografin for these duodenal segments. Water was not significantly different from 0.1% gastrografin with respect to the visualisation of the mucosal folds for any of the bowel segments.

The kappa value for bowel distension was 0.698 and that for the discrimination of bowel loops was 0.793, indicating a substantial agreement between the two observers. An almost perfect agreement between the two observers was achieved for mural visualisation (kappa value 0.890) and visualisation of mucosal folds (kappa value 0.874). No patient refused to drink the total prescribed amount of contrast agent in any of the three patient groups. Water and 0.1% gastrografin were well-tolerated, with no side effects documented. However, three of the 30 patients (10%) who

received 3.8% milk as oral contrast agent reported immediate post-test diarrhoea. Besides this, no other immediate or delayed side effects were communicated.

DISCUSSION

Adequate small bowel distension and good mural visualisation are important for the evaluation of small bowel disorders using MDCT. There are various factors that affect bowel distension and mural visualisation using this technique, and these include the volume of oral contrast ingested as well as the time between oral contrast ingestion and CT imaging. A larger volume of oral contrast, if tolerated by the patient, would no doubt provide better bowel distension. According to Young et al, the time to optimal distension of the terminal ileum is 51–72 minutes.[4] Hence, it is advised that the oral contrast agent be ingested about 60 minutes before CT imaging commences.

Bowel distension is also affected by the fat content and osmolarity of the oral contrast agent ingested. An oral contrast agent with a high fat content would decrease bowel peristalsis and delay gastrointestinal emptying, thus resulting in superior bowel distension.[5] Osmolarity of the oral contrast agent has also been reported to be a decisive parameter, as higher osmolarity would give a better degree of bowel distension.[6] Mural visualisation is mainly affected by the attenuation difference between the ingested oral contrast agent and the small bowel wall that is enhanced using an intravenous contrast material. Therefore, CT enterography combines neutral oral contrast agents with intravenous contrast for small bowel assessment. A neutral oral contrast agent is defined as a bowel-marking agent that gives bowel lumen attenuation either similar to or as near that of water, with a Hounsfield unit of zero. When a neutral oral contrast is used, the contrast-filled bowel lumen would appear hypodense in contrast to the bowel wall, which would appear hyperdense due to intravenous contrast enhancement. This attenuation difference subsequently makes any evidence of disease at the bowel wall more visible.

Water is a feasible oral contrast agent, as it is safe, cheap and well-tolerated. However, water is absorbed too rapidly in the stomach and proximal small bowel, and this limits its effectiveness for distension of the distal small bowel, which is the area most affected in Crohn's disease. Our study showed that water was significantly inferior for bowel distension and mural visualisation of the distal small bowel. Therefore, the use of water alone as an oral contrast agent without smooth muscle relaxants is unlikely to provide a satisfactory distal bowel assessment. Ajaj et al showed that there was a dose-response association between increasing osmolarity of the oral contrast agent and bowel distension, and the authors thus concluded that the osmolarity of the solution used plays a decisive role for small bowel distension.[7] While this view was supported by a later study by Borthne et al,[6] these authors also suggested a linear dose-response relationship between the level of osmolarity and the occurrence of adverse events.[6] Side effects such as distaste, nausea, vomiting, diarrhoea, flatulence and abdominal spasm were found to increase with increasing total ingested dose, and vice versa. Therefore, our goal was to look for a neutral oral contrast agent that had an osmolarity higher than that of water, but had minimal side effects. We postulated that 0.1% gastrografin could replace water as the neutral oral contrast agent while simultaneously obviating the need for smooth muscle relaxants. With a Hounsfield unit of 8–16, 0.1% gastrografin would provide bowel lumen attenuation that is nearly the same as that of water but with a concentration too low (0.1%) to produce any side effects.

Our results showed that 0.1% gastrografin was well-tolerated by patients, with none having any documented side effects. However, contrary to our hypothesis that 0.1% gastrografin, with an osmolarity higher than water, would give better bowel distension, our results showed otherwise. There was no significant difference between 0.1% gastrografin and water in terms of bowel distension, discrimination of bowel loops, mural visualisation and visualisation of mucosal folds. This was perhaps because a small difference in the total amount of osmotically active particles suspended in two different solutions of the same volume was unlikely to result in significantly different bowel distensions.

As opposed to water as a neutral oral contrast agent, 3.8% milk contains fat that effectively decreases peristalsis and slows passage through the gastrointestinal tract, thus resulting in superior bowel distension. In addition, 3.8% milk does not require the administration of a smooth muscle relaxant such as glucagon to achieve adequate bowel distension, and therefore eliminates potentially undesirable side effects and additional expenses. Our study showed that 3.8% milk was superior to both water and 0.1% gastrografin for bowel distension, discrimination of bowel loops, mural visualisation and visualisation of mucosal folds, mainly of the jejunum, ileum and terminal ileum, which are common sites of Crohn's disease. Therefore, 3.8% milk should be the preferred neutral oral contrast agent for CT enterography in patients with inflammatory bowel disease associated with Crohn's disease.

Among the patients who received 3.8% milk in our study, 10% had post-test diarrhoea, which was likely caused by lactose intolerance. The enzyme lactase is needed to break down lactose prior to absorption into the bloodstream, and in individuals deficient in this enzyme, there is a failure of proper lactose absorption from the bowel, which then causes symptoms such as bloating and diarrhoea. Lactose intolerance is known to be more common in certain ethnic and racial populations such as those of Asian descent, where milk is not traditionally part of the typical adult diet.[8-12] Some patients may not have symptoms when they consume a small amount of lactose. In our study, the patients' symptoms were triggered by the ingestion of a rather large amount of lactose (nearly 1 L of milk) before CT imaging. Further studies are required to explore alternative neutral oral contrast agents for use in patients who are lactose- or cow's milk-intolerant but require CT enterography.

This study has several limitations. Although three different groups of patients were assigned for the three different oral

contrast agents tested, it was difficult to eliminate the effects of interindividual variability. Repeating the CT examination using a different oral contrast agent in the three patient groups would not only expose these patients to unacceptably large doses of radiation, but it would also be deemed as unethical practice. Also, a standard volume of oral contrast agent (1 L) was applied for all patients regardless of body weight or size in order to avoid errors arising from inaccurate dosage calculation of contrast agents in the setting of a busy radiology department such as ours. While this study made the assumption that all patients included in the study were of standard adult body habitus, the authors recognise that larger patients would require a larger volume of oral contrast agent to obtain the same degree of bowel distension.

Apart from the above, a standard timing was also applied for oral contrast agent ingestion, which was an initial volume of 600 mL at 40–60 minutes before imaging and an additional 400 mL 20 minutes before imaging. However, as each patient would be expected to have a different rate of bowel peristalsis, it is possible that the timing of oral contrast administration was not optimal for all patients. Moreover, only qualitative evaluations of bowel distension were performed in this study, as previous studies have shown that qualitative assessments parallel quantitative measures.[13] Furthermore, to the authors' knowledge, there is no readily available existing method that would allow for a volumetric assessment of the entire gastrointestinal segment of interest. In addition, close supervision by radiology department personnel was required for the entire duration of oral contrast intake in our study, as timely access to a CT scanner once the contrast agent has been consumed is important. This may not necessarily be practical in other busy settings and may potentially limit the use of CT enterography in an outpatient population. Finally, our study population was also limited to patients who could largely tolerate lactose-containing milk. Further studies that use lactose-free milk for patients who are lactose- or cow's milk-intolerant but require CT enterography are thus warranted.

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